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Outcomes of surgical treatment of hemangiomas

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Abstract

Objective: Quantify complications and rates of adverse events associated with surgical excision of hemangiomas in children using a national surgical database.

Data source: Pediatric American College of Surgeons (ACS) National Surgical Quality Improvement Program® (ACS NSQIP® - pediatric), years 2012 – 2016.

Methods: Subjects included children under 18 years with a postoperative diagnosis of International Classification of Diseases (ICD), 9th revision code: 228.00 and 228.01, or ICD 10 codes D18.00 and D18.01– hemangioma, any site and hemangioma, of skin and subcutaneous tissue.

Results: A total of 1180 patients were included. The median age was 3.2 years [interquartile range (IQR) 1.2 to 6.4 years old. No occurrences of deep incisional SSI, nerve injury, mortality, sepsis, septic shock, or blood stream infections were noted. In multivariate analysis, age ≥ 3 years and advanced ASA class were significant predictors of adverse events ($p = 0.035$ and 0.001 , respectively).

Conclusions: For children with infantile hemangioma who fail to respond or have an incomplete response to medical therapy, surgical resection may be a relatively safe treatment alternative. Children older than 3 years of age with hemangiomas have less surgical adverse events than younger children. Overall, however, the surgical complications rates were low and deemed relatively minor.

Keywords

NSQIP; complications; hemangioma; vascular anomalies; surgery

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Introduction

Infantile hemangiomas (IH) are the most common tumors of childhood. Unlike other tumors, after a proliferative phase, they may exhibit involution to varying degrees. Primary care providers may often assume that these will resolve without intervention or consequence. However, a subset of these types of vascular tumors may be associated with complications, resulting in pain, functional impairment, or permanent disfigurement.¹ Historically, routine treatment options included expectant management with clinical re-evaluation, intralesional or systemic steroids, laser therapy, and/or surgical excision.^{2,3} In 2008, propranolol therapy was first reported and has emerged as a highly effective treatment with minimal side effects and has become the preferred option for active therapy.⁴⁻⁶ With excellent response rates to medical therapy, of upwards of above 90%, the decision to proceed with surgical excision must be taken cautiously and is often reserved for children refractory to medical or conservative treatment.⁷ Some concerns regarding the effects of propranolol on future cognitive development have been raised in very young children, but no effects of propranolol therapy on neurodevelopmental impairment in children have been demonstrated.⁸ There is little information at this time regarding updated surgical management of hemangiomas after widespread utilization of propranolol.

Methods

The American College of Surgeons (ACS) has developed a hospital based reporting system called the ACS National Surgical Quality Improvement Program® (ACS NSQIP®). Data were collected from the patient's medical chart, not insurance claims, and reports 30-day patient outcomes. Starting in 2012, participating children's hospitals began using this database and reporting results in the ACS NSQIP-pediatric® database. This database presents a unique opportunity to examine clinical factors that may be associated with 30-day adverse events related to surgical procedures in children. Duke University Institutional Review Board (IRB) approval exemption was obtained prior to initiating this investigation.

Patients were identified using a combination of postoperative diagnosis and 2016 current procedural terminology (CPT) codes. The following ICD-9 diagnosis codes 228.00 and 228.01, or ICD-10 code D18.00 and D18.01 were included: hemangioma, any site and hemangioma, of skin and subcutaneous tissue. These ICD-9/10 diagnosis codes were then cross-referenced against the CPT codes to identify those children who underwent surgical intervention for cutaneous facial/head and neck hemangiomas [11420 – 11424, 11426; 11440 – 11444, 11446], cutaneous non-head and neck hemangiomas [11400 – 11404, 11406], and all other procedures were classified as non-cutaneous hemangioma excisions.

The primary outcomes were adverse events, defined as: superficial incisional surgical site infection (SSI), deep incisional SSI, organ space SSI, superficial wound disruption, wound disruption, pneumonia, unplanned intubation, unplanned reoperation, readmission, nerve injury, prolonged hospitalization (> 30 days), sepsis, septic shock, bleeding with transfusion, bloodstream infection, and mortality.

Summary data regarding demographic information were collected. Categorical variables are summarized with frequency counts and percentages. Continuous variables are summarized with means, standard deviations, median, interquartile ranges (IQR) and ranges. Clinical risk factors that we assessed can be found in Table 1. These factors were examined for association with adverse events. Patients were divided into two groups, based on the presence of an adverse event. Differences between the two groups were assessed using Wilcoxon-Mann-Whitney tests for continuous variables, and Chi-square or Fisher's exact tests for categorical variables. Additionally, multivariate logistic regression analysis was performed to model the probability of experiencing an adverse event with clinical risk factors as covariates. Throughout this work, the threshold for assessing statistical significance was set at level $\alpha = 0.05$, and all analyses were performed using SAS 9.4 statistical software (SAS Institute Inc., Cary, NC).

Results

A total of 1180 patients were included; some children underwent multiple concurrent excisions in both head and neck areas as well as other areas of the body. Demographic information is summarized in Table 2. The median age was 3.2 years (IQR 1.2 to 6.4 years old).

The frequency and percentage of adverse events stratified by head/neck cutaneous excision procedures are summarized in Table 3. No occurrences of deep incisional SSI, nerve injury, mortality, sepsis, septic shock, or blood stream infections were noted. For patients who had only head and neck cutaneous excision procedures, 4.1% (29/709) had adverse events. For patients who had cutaneous excision procedures on other body regions, 3.5% (12/342) had adverse events. Patients who had cutaneous excision procedures on both head/neck and other regions did not have any identified adverse events. For patients who had other non-cutaneous excision procedures, 6% (6/100) had adverse events. There was no significant difference in the occurrence of adverse events between head/neck group and the group with procedures in other body regions ($p = 0.648$).

Frequency and percentage of procedure sizes were examined based on anatomic location: isolated head and neck versus other isolated body area. Patients with concurrent excisions in both anatomic areas, and those with multiple procedures in the same body area but different sizes were excluded to strictly compare the two distinct anatomic areas. These are summarized in Table 4. Based on size, lesions < 0.5 cm had the lowest percentage of adverse event (1.3%), and size 2.1–3 cm and size 3.1–4 cm had the highest percentage of adverse event (6.0%, 5.6%, respectively). Size of excision did not significantly impact adverse events ($p = 0.270$).

Demographic information and risk factors stratified by adverse event are summarized in Table 5. Clinical factors that were considered as candidate risk factors of adverse events included: age less than 3 years old, inpatient setting, prematurity, bronchopulmonary dysplasia/chronic lung disease, structural pulmonary/airway abnormality, cardiac disease, steroid use, and congenital malformations. The median age of patients who had adverse events was 1.8 years (IQR 0.8 to 4.2 years old), and the median age of patients who did not

have adverse events was 3.3 years (IQR 1.2 to 6.6 years old). 30 out of 564 patients (5.3%) with age ≤ 3 years had significantly more adverse events, while 17 out of 616 patients (2.8%) with age > 3 years had adverse events, $p = 0.026$. Younger patients tended to have higher percentage of adverse events, but we also found that patients aged 5, 7, and 13 had adverse event rate 5% or above. Note that there was only one patient with an adverse event in age 13 group; and because the small sample size in this group, the adverse event rate is above 5%.

Multivariable logistic regression was used to assess the association of candidate risk factors with adverse event, and the estimated odds ratios, 95% confidence intervals, and p-values are presented in Table 6. Age was a significant predictor ($p = 0.035$). The odds of having adverse events for patients who were ≤ 3 years old were 1.94 fold of the odds for patients who were > 3 years old (odds ratio [OR] 1.94, 95% CI: 1.05 to 3.58). ASA class was also a significant predictor ($p = 0.0012$). The odds of having adverse events for patients who were in ASA groups 2 – 4 were 2.69 fold of the odds for patients who were in ASA 1 group (OR 2.70, 95% CI: 1.48 to 4.91). Wound contamination was a marginal predictor ($p = 0.051$). The odds of having adverse events for patients who had contaminated wounds was 2.07 fold of the odds for patients who had clean wounds (OR 2.07, 95% CI: 1.00 to 4.31).

Discussion

This study examines adverse events related to surgical excision of hemangiomas in children in the timeframe after widespread adoption of propranolol therapy for infantile hemangiomas. Overall, the rate of adverse events was fairly low. We did not identify any serious adverse events, such as mortalities, cases of nerve injuries or systemic infections. Most were relatively minor and related to unplanned re-operations, re-admissions, and wound infections or disruptions. No prior investigations or published guidelines exist at this time as a target for acceptable adverse event rates for these types of surgical procedures; however, it would be reasonable that the expected and acceptable rate would be targeted at less than 5% and our findings are consistent with this. No significant difference in adverse events was noted between head and neck region and other parts of the body, nor with size of the excision ($p = 0.648$ and 0.270 , respectively). Clinical risk factors that were associated with higher rates of adverse events included: median age, inpatient setting, prematurity, bronchopulmonary dysplasia/chronic lung disease, structural pulmonary/airway abnormality, cardiac disease, steroid use, congenital malformations, nutritional support, hematologic disorder, contaminated wound, emergent/urgent case status, and advanced ASA status (2–4). More medically fragile children, as reflected by ASA status, should be referred for surgery with caution and only if risk for functional or life-threatening compromise.

Of notable interest, we found that younger children tended to have higher rates of adverse events (mean of 1.8 years versus 3.3 years; age ≤ 3 years was noted to be a significant risk factor in multivariate analysis, $p = 0.0347$), and age should potentially impact decision making regarding timing of surgical therapy. The optimal timing for surgery of hemangiomas in young children has been examined, accounting for the biological behavior of these tumors, facial development and reconstructive considerations, and knowledge of developmental psychology on social and self-image/confidence concerns.⁹ The authors

recommended that efforts should be made to obtain the best possible clinical outcomes with treatment by age 3 but if other circumstances arise, results should be finalized before the child enters formal schooling, around 5 to 6 years of age. Caution should be taken with our findings, as we were not able to differentiate hemangiomas that were causing functional limitations and were not able to take into account the psychological aspects of surgical timing.

One significant limitation inherent to a retrospective study using a national database is accurate, appropriate diagnosis and coding, as there is no ICD-9 or ICD-10 code that specifies IH from congenital hemangiomas. However, in clinical practice, IH are by far the most common type of hemangioma seen. Thus, it is extremely likely that the cases we captured were primarily IH. Specific location in the head and neck region and other body areas was also not able to be ascertained. There are specific anatomic locations in the head and neck that may be associated with more unfavorable and unsatisfactory outcomes, with earlier intervention advocated to achieve better outcomes.¹⁰ Also lacking, is an ability to track individual patient outcomes to help develop recommendations for patient selection and timing, along with limited follow up and outcome measures for treatment effectiveness. The best candidates for elective surgery may be those with localized eyelid, nasal, or lip hemangiomas, presenting with growth-related deformities during the proliferative phase.¹¹ Severity of disease and clinical presentation for individual cases could not be ascertained using this database approach; thus, it is not possible to determine which patients were selected for surgery.

Complicated lesions are best managed in a multidisciplinary fashion.¹² For children with infantile hemangioma who fail to respond or have an incomplete response to medical therapy, surgical resection may be a relatively safe treatment alternative. Children older than 3 years of age with hemangiomas have less surgical adverse events than younger children. Overall, however, the surgical complications rates were low and deemed relatively minor.

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Table 1.

Related clinical factors examined for impact on adverse events.

Age
Gender
Race (American Indian, Asian, Black or African American, Native Hawaiian, White, Unknown)
Case status (inpatient/outpatient)
Premature birth
Asthma
History of chronic lung disease or prematurity/bronchopulmonary dysplasia
Tracheostomy (yes/no)
Structural pulmonary/airway abnormalities
Cardiac risk factors
Developmental delay/impaired cognitive status
Seizure disorder
Cerebral palsy
Structural central nervous system abnormality
Neuromuscular disorder
Steroid use
Nutritional support
Hematologic disorder
Sepsis/septic shock within 48 hours prior to surgery
Congenital malformation
Case type (elective, emergent, or urgent)
Wound classification
American Society of Anesthesiologists (ASA) classification

Table 2.

Demographic information for patients with hemangiomas

	Head/Neck (N=709)	Head/Neck and Other Regions (N=29)	Other Body Regions (N=342)	Others (N=100)	Total (N=1180)
Gender					
Female	444 (62.6%)	16 (55.2%)	211 (61.7%)	72 (72.0%)	743 (63.0%)
Male	265 (37.4%)	13 (44.8%)	131 (38.3%)	28 (28.0%)	437 (37.0%)
Race					
White	528 (74.5%)	25 (86.2%)	258 (75.4%)	71 (71.0%)	882 (74.7%)
Black or African American	59 (8.3%)	2 (6.9%)	35 (10.2%)	10 (10.0%)	106 (9.0%)
Others	122 (17.2%)	2 (6.9%)	49 (14.4%)	19 (19.0%)	192 (16.3%)
Hispanic Ethnicity					
Missing	56 (.%)	1 (.%)	33 (.%)	7 (.%)	97
No	543 (83.2%)	26 (92.9%)	257 (83.2%)	67 (72.0%)	893 (82.5%)
Yes	110 (16.8%)	2 (7.1%)	52 (16.8%)	26 (28.0%)	190 (17.5%)
Age in Year					
Mean (SD)	4.1 (3.8)	4.1 (3.4)	5.4 (4.7)	4.5 (4.3)	4.5 (4.2)
Median	2.9	3.4	4.1	3.2	3.2
Q1, Q3	1.2, 5.5	1.2, 5.1	1.4, 8.3	1.2, 6.7	1.2, 6.4
Range	(0.0–17.7)	(0.4–13.2)	(0.0–17.7)	(0.2–17.3)	(0.0–17.7)
Inpatient/outpatient					
Inpatient	23 (3.2%)	0 (0.0%)	17 (5.0%)	21 (21.0%)	61 (5.2%)
Outpatient	686 (96.8%)	29 (100.0%)	325 (95.0%)	79 (79.0%)	1119 (94.8%)

Table 3.

Adverse events.

	Head/Neck (N=709)	Head/Neck and Other Regions (N=29)	Other Body Regions (N=342)	Others (N=100)	Total (N=1180)
Adverse Event	29 (4.1%)	0 (0.0%)	12 (3.5%)	6 (6.0%)	47 (4.0%)
Occurrences Superficial Incisional SSI	4 (0.6%)	0 (0.0%)	4 (1.2%)	0 (0.0%)	8 (0.7%)
Occurrences Organ/Space SSI	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (0.1%)
Occurrences Superficial Wound Disruption	12 (2.2%)	0 (0.0%)	6 (2.2%)	1 (1.2%)	19 (2.0%)
Occurrences Wound Disruption	3 (0.4%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	4 (0.3%)
Occurrences Pneumonia	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.1%)
Occurrences Unplanned Intubation	1 (0.1%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	2 (0.2%)
Unplanned Reoperation	10 (1.4%)	0 (0.0%)	3 (0.9%)	2 (2.0%)	15 (1.3%)
Readmission	11 (1.6%)	0 (0.0%)	2 (0.6%)	3 (3.0%)	16 (1.4%)
Still in Hospital > 30 Days	1 (0.1%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	2 (0.2%)
Occurrences Bleeding/Transfusion	1 (0.1%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	3 (0.3%)

Table 4.

Summary of size of cutaneous excisions, isolated facial/head and neck location compared to isolated other body region

Size	Head/Neck (N=689)	Other Body Regions (N=330)	Total (N=1019)
<0.5 cm	62 (9.0%)	13 (3.9%)	75 (7.4%)
0.6–1 cm	93 (13.5%)	27 (8.2%)	120 (11.8%)
1.1–2 cm	200 (29.0%)	63 (19.1%)	263 (25.8%)
2.1–3 cm	145 (21.0%)	56 (17.0%)	201 (19.7%)
3.1–4 cm	86 (12.5%)	40 (12.1%)	126 (12.4%)
>4 cm	103 (14.9%)	131 (39.7%)	234 (23.0%)

Table 5.

Clinical risk factors for adverse events.

Adverse Event	No (N=1133)	Yes (N=47)	Total (N=1180)
Gender			
Female	711 (62.8%)	32 (68.1%)	743 (63.0%)
Male	422 (37.2%)	15 (31.9%)	437 (37.0%)
Race			
American Indian or Alaska Native	3 (0.3%)	0 (0.0%)	3 (0.3%)
Asian	20 (1.8%)	0 (0.0%)	20 (1.7%)
Black or African American	106 (9.4%)	0 (0.0%)	106 (9.0%)
Native Hawaiian or Other Pacific Islander	2 (0.2%)	0 (0.0%)	2 (0.2%)
Unknown/Not Reported	155 (13.7%)	12 (25.5%)	167 (14.2%)
White	847 (74.8%)	35 (74.5%)	882 (74.7%)
Age in Year			
N	1133	47	1180
Mean (SD)	4.6 (4.2)	2.9 (3.1)	4.5 (4.2)
Median	3.3	1.8	3.2
Q1, Q3	1.2, 6.6	0.8, 4.2	1.2, 6.4
Range	(0.0–17.7)	(0.0–13.9)	(0.0–17.7)
Inpatient/outpatient			
Inpatient	54 (4.8%)	7 (14.9%)	61 (5.2%)
Outpatient	1079 (95.2%)	40 (85.1%)	1119 (94.8%)
Premature Birth			
Missing	113	5	118
25–26 completed weeks gestation	14 (1.4%)	0 (0.0%)	14 (1.3%)
27–28 completed weeks gestation	16 (1.6%)	1 (2.4%)	17 (1.6%)
29–30 completed weeks gestation	16 (1.6%)	0 (0.0%)	16 (1.5%)
31–32 completed weeks gestation	29 (2.8%)	3 (7.1%)	32 (3.0%)
33–34 completed weeks gestation	40 (3.9%)	0 (0.0%)	40 (3.8%)
35–36 completed weeks gestation	76 (7.5%)	4 (9.5%)	80 (7.5%)
History Asthma	51 (4.5%)	2 (4.3%)	53 (4.5%)
Bronchopulmonary Dysplasia/Chronic Lung disease	14 (1.2%)	2 (4.3%)	16 (1.4%)
Tracheostomy	3 (0.3%)	0 (0.0%)	3 (0.3%)
Structural pulmonary/airway abnormality	14 (1.2%)	2 (4.3%)	16 (1.4%)
Cardiac risk factors			
Major cardiac risk factors	7 (0.6%)	3 (6.4%)	10 (0.8%)
Minor cardiac risk factors	25 (2.2%)	0 (0.0%)	25 (2.1%)
No cardiac risk factors	1100 (97.1%)	44 (93.6%)	1144 (96.9%)
Severe cardiac risk factors	1 (0.1%)	0 (0.0%)	1 (0.1%)
Developmental delay/impaired cognitive status	43 (3.8%)	2 (4.3%)	45 (3.8%)
Seizure Disorder	7 (0.6%)	1 (2.1%)	8 (0.7%)

Adverse Event	No (N=1133)	Yes (N=47)	Total (N=1180)
Structural CNS Abnormality	15 (1.3%)	1 (2.1%)	16 (1.4%)
Neuromuscular Disorder	2 (0.2%)	1 (2.1%)	3 (0.3%)
Steroid use (within 30 days)	5 (0.4%)	1 (2.1%)	6 (0.5%)
Nutritional support	4 (0.4%)	3 (6.4%)	7 (0.6%)
Hematologic Disorder	3 (0.3%)	3 (6.4%)	6 (0.5%)
SIRS/Sepsis/Septic Shock within 48 hours prior to surgery	1 (0.1%)	0 (0.0%)	1 (0.1%)
Congenital Malformation			
Yes, Neonate < 1500 grams at the time of surgery	2 (0.2%)	1 (2.1%)	3 (0.3%)
Yes, Neonate >=1500 grams at the time of surgery or infant/child/teenager with a history of a congenital defect at the time of surgery	519 (45.8%)	25 (53.2%)	544 (46.1%)
Case Status			
Elective	1121 (98.9%)	43 (91.5%)	1164 (98.6%)
Emergent	3 (0.3%)	3 (6.4%)	6 (0.5%)
Urgent	9 (0.8%)	1 (2.1%)	10 (0.8%)
Wound classification			
Clean	1003 (88.5%)	37 (78.7%)	1040 (88.1%)
Clean/Contaminated	123 (10.9%)	8 (17.0%)	131 (11.1%)
Contaminated	6 (0.5%)	2 (4.3%)	8 (0.7%)
Dirty/Infected	1 (0.1%)	0 (0.0%)	1 (0.1%)
ASA classification			
Missing	8	0	8
ASA 1 - No Disturb	737 (65.5%)	19 (40.4%)	756 (64.5%)
ASA 2 - Mild Disturb	362 (32.2%)	21 (44.7%)	383 (32.7%)
ASA 3 - Severe Disturb	25 (2.2%)	5 (10.6%)	30 (2.6%)
ASA 4 - Life Threat	1 (0.1%)	2 (4.3%)	3 (0.3%)

Table 6.

Multivariate regression analysis for clinical risk factors and adverse events. A multivariate logistic regression was used to model the probability of occurrence of adverse events as a function of the following variables: age group (≤ 3 years, >3 years), congenital malformation and/or prematurity (yes, no), wound contamination (clean, contaminated), and ASA class (ASA class 1, ASA class 2–4). Age ≤ 3 years and less had 534 children with 30 (5.3%) adverse events, and there were 599 children with 17 (2.8%) adverse events in the cohort of children over 3 years of age.

Effect	Odds Ratio Estimate [95% Wald Confidence Limits]	p-value
Age ≤ 3 years vs. >3 years	1.939 [1.049 – 3.584]	0.0347
Congenital malformation and/or Prematurity	1.246 [0.685 – 2.264]	0.4715
Wound class	2.074 [0.997 – 4.314]	0.0508
ASA class 2–4	2.694 [1.478 – 4.911]	0.0012